

**Initial REMS Approval: 09/25/2012**  
**Most Recent Modification: 09/2013**

## **RISK EVALUATION AND MITIGATION STRATEGY (REMS)**

### **Single Shared System for Mycophenolate**

## **I. GOALS**

The goals of the Mycophenolate REMS are:

1. To prevent unplanned pregnancy in patients using mycophenolate and to minimize fetal exposure to mycophenolate by informing prescribers and females of reproductive potential about:
  - the increased risk of first trimester pregnancy loss and congenital malformation associated with exposure to mycophenolate during pregnancy; and
  - the importance of pregnancy prevention and planning
2. To minimize the risks associated with fetal exposure to mycophenolate by collecting information on pregnancy outcomes through the Mycophenolate Pregnancy Registry
3. To inform patients about the serious risks associated with mycophenolate.

## **II. REMS ELEMENTS**

### **A. Medication Guide**

A Medication Guide will be dispensed with each mycophenolate prescription in accordance with 21 CFR 208.24.

The Medication Guides for mycophenolate-containing products are part of the Mycophenolate REMS and will be available on the Mycophenolate REMS website ([www.MycophenolateREMS.com](http://www.MycophenolateREMS.com)).

### **B. Elements to Assure Safe Use**

#### **1. Healthcare providers who prescribe mycophenolate will receive training.**

- a) Mycophenolate sponsors will ensure that training will be provided to healthcare providers who prescribe mycophenolate-containing products. To become trained, each prescriber will be provided with the *Mycophenolate Program Brochure for Healthcare Providers*. The brochure includes the following information:
  - i. The risk of first trimester pregnancy loss and congenital malformations associated with mycophenolate
  - ii. Importance of educating females of reproductive potential about the increased risk of first trimester pregnancy loss and congenital malformations associated with exposure to mycophenolate during pregnancy
  - iii. Importance of prescribers providing or facilitating patient education about pregnancy prevention and planning, including acceptable methods of contraception during mycophenolate treatment

- iv. Importance of only prescribing mycophenolate to a pregnant patient if the benefits of initiating or continuing treatment outweigh the risk of fetal harm
  - v. Importance of reporting to the Pregnancy Registry any pregnancies that occur during mycophenolate treatment or within 6 weeks following discontinuation of treatment
  - vi. Importance of encouraging pregnant patients to participate in the Pregnancy Registry
  - vii. Importance of obtaining a signed *Patient-Prescriber Acknowledgement Form* from each female of reproductive potential. The *Patient-Prescriber Acknowledgement Form* is part of the Mycophenolate REMS and is appended
- b) Mycophenolate sponsors will ensure that prescribers can successfully report that they have taken the training via the Mycophenolate REMS website, mail, fax, or by scanning and e-mailing the *Prescriber Training Confirmation Form*. The *Prescriber Training Confirmation Form* is part of the Mycophenolate REMS and is appended.
  - c) Mycophenolate sponsors will maintain a list of all healthcare providers (HCPs) who have completed the Mycophenolate REMS Training.
  - d) Mycophenolate sponsors will redistribute the training materials every two years or following substantive changes that affect the Mycophenolate REMS. Substantive changes are defined as 1) significant changes to the operation of the Mycophenolate REMS; 2) changes to the *Prescribing Information* and *Medication Guide* that affect the risk-benefit profile of mycophenolate.
  - e) Mycophenolate sponsors will provide educational materials and a *DHCP Letter for Centers* to centers (e.g., transplant centers) that choose to administer training to their prescribers through their own centralized process. Mycophenolate sponsors will ensure that a designee of the Center can successfully report the healthcare providers who have participated in the training via the Mycophenolate REMS website, mail, fax, or by scanning and e-mailing the *Center Training Confirmation Form*.

The *Center Training Confirmation Form* is part of the Mycophenolate REMS and is appended. The *DHCP Letter for Centers* is part of the Mycophenolate REMS and is appended.
  - f) Mycophenolate sponsors will submit for publication a *Journal Information Piece* in the following journals:
    - Transplantation
    - American Journal of Transplantation
    - Neurology
    - Arthritis & Rheumatism
    - Journal of the American Academy of Dermatology
    - Journal of the American Society of Nephrology

- Obstetrics and Gynecology
- Pediatrics
- American Family Physician

This piece is designed to convey the risks of mycophenolate products, the importance of completing the training, and details on where and how educational materials can be accessed. It will appear monthly for the first 6 months after FDA approval of the REMS and every other month in the subsequent 6 months.

The *Journal Information Piece* is part of the Mycophenolate REMS and is appended.

- g) Mycophenolate sponsors will ensure that no later than 8 weeks after approval of the REMS, a *Dear Healthcare Professional (DHCP) Introductory Letter* will be sent to all HCPs who prescribed mycophenolate in the 24 months preceding REMS approval, accompanied by program materials (Prescriber Kit and Patient Kit).

Mycophenolate sponsors will ensure that no later than 8 weeks after approval of the REMS, a *DHCP Introductory Letter* will be sent to all HCPs who: are on the following American Medical Association subspecialty lists: allergy and immunology, immunology, cardiology, dermatology [including surgery, and dermatopathology], gastroenterology, neurology [including surgery and neuropathology], OB/GYN [including maternal fetal medicine], general surgery, thoracic surgery, transplantation surgery, hepatology, nephrology, and rheumatology and all corresponding pediatric subspecialties, and; have not prescribed mycophenolate in the 24 months preceding REMS approval. The *DHCP Introductory Letter* is designed to convey and reinforce the increased risks of first trimester pregnancy loss and congenital malformation associated with mycophenolate exposure during pregnancy and the importance of prescribers completing the training and will include important safety information about products that contain mycophenolate. The *DHCP Introductory Letter* will also provide details on where and how educational materials can be ordered. The letter will be available on the Mycophenolate REMS website for 1 year from the date of distribution.

The *DHCP Introductory Letter* is part of the Mycophenolate REMS and is appended.

- h) Mycophenolate sponsors will maintain a call center to support prescribers interfacing with the Mycophenolate REMS.
- i) Mycophenolate sponsors will monitor distribution and prescription data monthly to identify new prescribers who should be trained.

- j) The following materials are part of the Mycophenolate REMS and are appended:
- *Mycophenolate REMS Brochure for Healthcare Providers*
  - *Patient-Prescriber Acknowledgement Form*
  - *Prescriber Training Confirmation Form*
  - *Center Training Confirmation Form*
  - *DHCP Letter for Centers*
  - *Journal Information Piece*
  - *DHCP Introductory Letter*
  - *Obstetrician/Gynecologist Referral Template Letters for Contraception Counseling*
  - *Obstetrician/Gynecologist Referral Template Letters for Preconception Counseling*
  - *Mycophenolate REMS Overview for Patients and Your Birth Control Options*
  - *Mycophenolate Pregnancy Registry Frequently Asked Questions for Patients*
  - *Mycophenolate REMS Website*

These materials will also be available on the Mycophenolate REMS website or by calling the Mycophenolate REMS call center at 1-800-617-8191.

**2. Mycophenolate sponsors will maintain a centralized pregnancy registry for females who become pregnant and consent to participate.**

The primary objectives of the Pregnancy Registry are to:

- Document maternal and fetal outcomes of each exposed pregnancy to further characterize the risk of mycophenolate fetal exposure.
- Determine mycophenolate exposure status for each reported pregnancy
- Understand the circumstances that led to the fetal exposure (root cause analysis)
- Identify factors that affect the risk of adverse outcomes such as dose, timing of exposure, or maternal characteristics

**III. Timetable for Submission of Assessments**

Mycophenolate NDA sponsors will submit REMS assessments to FDA every 6 months for the first year from the date of initial approval of the Mycophenolate REMS and annually thereafter. To facilitate inclusion of as much information as possible while allowing reasonable time to prepare the submission, the reporting interval covered by

each submission will conclude no earlier than 60 days before the submission date for that assessment. The assessment will be submitted so that it is received by the FDA on or before the due date.

# BROCHURE FOR HEALTHCARE PROVIDER





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## Introducing Mycophenolate REMS

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(Risk Evaluation and Mitigation Strategy)  
FDA (Food and Drug Administration)  
data showing that exposure to  
pregnancy is associated with increased risks  
of pregnancy loss and congenital malformations.  
In clinical studies, structural malformations occur in  
approximately 20% of live-born infants exposed in utero to  
mycophenolate. Pregnancy loss rates are higher.\*†  
Based on this information, it is concluded that a REMS is necessary to ensure that the  
benefits outweigh the risks of first trimester  
congenital malformations associated with  
pregnancy.

Available by prescription as:  
Mycophenolate mofetil  
(mycophenolic acid)  
Mycophenolate sodium  
(mycophenolic acid)

### The goals of the Mycophenolate REMS are:

1. To prevent unplanned pregnancy in patients using mycophenolate and to minimize fetal exposure to mycophenolate by informing prescribers and females of reproductive potential about:
  - The increased risks of first trimester pregnancy loss and congenital malformations associated with exposure to mycophenolate during pregnancy; and
  - The importance of pregnancy prevention and planning
2. To minimize the risks associated with fetal exposure to mycophenolate by collecting information on pregnancy outcomes through the Mycophenolate Pregnancy Registry
3. To inform patients about the serious risks associated with mycophenolate

comes in solid organ transplant recipients with exposure to mycophenolate mofetil or sirolimus.  
02.  
mycophenolate.

For more information, please see full *Prescribing Information*, including **Boxed WARNING** and *Medication Guide*, which can be found at [mycophenolateREMS.com](http://mycophenolateREMS.com)



## Introducing Mycophenolate REMS (cont'd)

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nolate and females of reproductive potential, whether or not they plan to get pregnant, should be ated with mycophenolate.

**potential** include girls who have men who have a uterus and have not se.

the permanent end of menstruation and fertility.

cally confirmed by a patient's healthcare only used diagnostic criteria include: taneous amenorrhea (not amenorrhea medical condition or medical therapy); or om a bilateral oophorectomy

This brochure, the *Mycophenolate REMS Brochure for Healthcare Providers*, has been designed to help you understand the components of Mycophenolate REMS. Included are details on what you can do to help ensure the successful implementation of Mycophenolate REMS so that patients understand the risks associated with exposure to mycophenolate during pregnancy.

## ted First Trimester Pregnancy Loss and Congenital Malformations

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fetal harm when administered  
female. Exposure to mycophenolate during  
th an increased risk of:  
cy loss  
s (especially external ear and  
cleft lip and palate)  
s of the distal limbs, heart, esophagus and

2006, the National Transplantation  
R) published data from  
4 female transplant patients  
e-exposed pregnancies.\*

Of these pregnancies, there were:

s (45%)

live-born infants had structural malformations

to systemic mycophenolate  
re reported in postmarketing  
995 and 2007):  
bortions  
d fetus or infant  
malformed offspring had ear abnormalities

The reported malformations were similar to findings in  
animal reproductive toxicology studies. For comparison,  
background rate for congenital anomalies in the United  
States is about 3% and the NTPR data show a rate of 4%  
to 5% among babies born to organ-transplant patients  
using other immunosuppressive drugs. Because these  
postmarketing data are reported voluntarily, it is not  
always possible to reliably estimate the frequency of  
particular outcomes.

When initiating or continuing treatment with  
mycophenolate, you should educate females of  
reproductive potential on the risks associated with  
exposure to mycophenolate during pregnancy. They  
need to make informed decisions about treatment.

comes in solid organ transplant recipients with exposure to mycophenolate mofetil or sirolimus.  
02.  
henolate.



## Your Role in Mycophenolate REMS

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te the following steps to help ensure  
ion of Mycophenolate REMS  
ctive potential:

### **cophenolate REMS**

#### **Status**

#### **males of Reproductive Potential**

#### ***Patient-Prescriber Acknowledgment***

#### **cophenolate-Exposed Pregnancies**

### **cophenolate REMS**

You should become familiar with the risks of embryofetal toxicity  
olate and the requirements of

rehensive description of the  
e of mycophenolate.

As a prescriber of mycophenolate, you should enroll in  
Mycophenolate REMS by completing a *Prescriber  
Training Confirmation Form* to document that you  
understand, and will comply with Mycophenolate REMS.

You can submit a *Prescriber Training Confirmation Form*  
to Mycophenolate REMS by one of several ways:

- Visit [www.MycophenolateREMS.com](http://www.MycophenolateREMS.com) and complete the online form
- Complete a hard copy and submit it via fax to **1-800-617-5768**
- Complete a hard copy and mail it to:  
Mycophenolate REMS  
200 Pinecrest Plaza  
Morgantown, WV 26505-8065
- Call **1-800-617-8191**

## Your Role in Mycophenolate REMS (cont'd)

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### Pregnancy Status

Determine if females of reproductive potential

One pregnancy test with a sensitivity of at least 25 mIU/mL done immediately before

Another pregnancy test with the same sensitivity 8 to 10 days later. These tests should be performed at routine follow-up visits.

These tests should be discussed with the patient.

In the event of a positive pregnancy test, discuss the risks of treatment with the patient. The patient should be informed of the potential hazard to the fetus. In certain cases, the patient may decide the maternal risks to the fetus.

### Educate Females of Reproductive Potential

Discuss the risks of mycophenolate during pregnancy.

When starting or continuing treatment, you must inform females of reproductive potential by discussing with them the increased risks of first trimester and congenital malformations associated with mycophenolate during pregnancy. This information is shared in this presentation and is reinforced by the *Mycophenolate & Your Birth Control Options* booklet.

#### ■ Provide females of reproductive potential with a *Mycophenolate REMS Overview & Your Birth Control Options* booklet.

You should ensure that they understand their role in Mycophenolate REMS.

#### ■ Provide pregnancy planning education

Advise patients using mycophenolate to let you know if they are considering pregnancy. For a patient considering pregnancy, determine whether there are appropriate treatment options with less potential for embryofetal toxicity. In addition, it is important to optimize the patient's underlying medical condition(s) and nutritional status prior to conception. Refer patients for pre-conception counseling and high risk obstetrical care as needed and coordinate care among the patient's established providers.

#### ■ Provide contraception counseling

Unless patients choose not to have sexual intercourse with a man at any time (abstinence), you must instruct them to always use acceptable contraception:

- During entire treatment with mycophenolate
- For 6 weeks after they stop taking mycophenolate



## Your Role in Mycophenolate REMS (cont'd)

The following table lists the forms of contraception that are acceptable for use during treatment with mycophenolate. Guide your patients to choose from the following birth control options:

Acceptable Contraception Methods for Females of Reproductive Potential*			
Option 1	<ul style="list-style-type: none"><li>■ Intrauterine devices (IUDs)</li><li>■ Tubal sterilization</li><li>■ Patient's partner had a vasectomy</li></ul>		
Methods to Use Alone			
OR			
Option 2	Hormone Methods choose 1		Barrier Methods choose 1
Choose One Hormone Method AND One Barrier Method	<b>Estrogen and Progesterone</b> <ul style="list-style-type: none"><li>■ Oral contraceptive pill</li><li>■ Transdermal patch</li><li>■ Vaginal ring</li></ul> <b>Progesterone-only</b> <ul style="list-style-type: none"><li>■ Injection</li><li>■ Implant</li></ul>	AND	<ul style="list-style-type: none"><li>■ Diaphragm with spermicide</li><li>■ Cervical cap with spermicide</li><li>■ Contraceptive sponge</li><li>■ Male condom</li><li>■ Female condom</li></ul>
OR			
Option 3	Barrier Methods choose 1		Barrier Methods choose 1
Choose One Barrier Method from each column ( <i>must choose two methods</i> )	<ul style="list-style-type: none"><li>■ Diaphragm with spermicide</li><li>■ Cervical cap with spermicide</li><li>■ Contraceptive sponge</li></ul>	AND	<ul style="list-style-type: none"><li>■ Male condom</li><li>■ Female condom</li></ul>

\*Females of reproductive potential include girls who have entered puberty and all women who have a uterus and have not passed through menopause.

## Your Role in Mycophenolate REMS (cont'd)

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### EMERGENCY CONTRACEPTION

Patients should also be counseled on the availability of emergency contraception in the event they have reliable contraception or their methods fail. Patients 17 years and older may obtain emergency contraception over the counter. Patients should call the Emergency Contraception Hotline (1-888-668-2528) to get information about emergency contraception.

REMS is neither affiliated with nor an endorser of this information provided by Mycophenolate REMS or this information for informational purposes only, and is not intended to replace medical advice to your patients.

#### ***Patient-Prescriber***

##### ***Acknowledgment Form***

After you have educated females of reproductive potential about the risk of exposure to mycophenolate, you should counsel them on family planning, have them sign the form, and a *Patient-Prescriber*

After the form is completed, patients agree that they will comply with the requirements. For patients who are unable to sign, a guardian should sign in addition to the patient. You too, as the prescriber, should sign the form and give a copy to the patient.

Keep a copy for your records.

### 5. Report any pregnancies to the Mycophenolate Pregnancy Registry

The Mycophenolate Pregnancy Registry has been established to evaluate mycophenolate-exposed pregnancies and their outcomes. This will provide an opportunity to learn more about mycophenolate exposure in utero.

Instruct patients to tell you if they get pregnant during treatment with mycophenolate or within 6 weeks following discontinuation of treatment. If you learn that a patient is pregnant:

- Report the pregnancy to the Mycophenolate Pregnancy Registry
  - By phone: **1-800-617-8191**
  - Online: [www.MycophenolatePregnancyRegistry.com](http://www.MycophenolatePregnancyRegistry.com); or
  - By mail:  
Mycophenolate Pregnancy Registry  
201 Broadway, Suite 5  
Cambridge, MA 02139



## Reporting a Pregnancy

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ed that you will report any  
of which you become aware to the  
Registry. Provision of patient  
medical information to the Mycophenolate  
red by an HIPAA waiver.

ancy Registry program administrator will  
lly identifiable pregnancy data to the appropriate drug  
of reporting to regulatory agencies as  
de-identified data may be shared  
sors of Mycophenolate REMS and/or  
peer-reviewed scientific journals.

Encourage the patient to participate in the  
ncy Registry

*Mycophenolate Pregnancy Registry  
ns for Patients*



## Frequently Asked Questions About Mycophenolate REMS and the Mycophenolate Pregnancy Registry

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### **Who can participate in the Mycophenolate REMS for?**

signed to help inform  
patients, and females of reproductive  
age who are exposed to mycophenolate

### **Who can participate in the Mycophenolate Pregnancy Registry?**

Patients who are pregnant or  
became pregnant while taking  
mycophenolate are eligible if she meets either  
one of the following criteria:  
• Pregnant and was exposed to  
mycophenolate during pregnancy  
• Pregnant within 6 weeks following  
discontinuation of treatment  
Patients who do not meet  
these criteria, regardless of  
whether they are currently  
pregnant, may not participate in the  
Mycophenolate Pregnancy Registry.

### **What are the goals of the Mycophenolate Pregnancy Registry?**

The goal of the Mycophenolate Pregnancy Registry is  
to collect data on the outcomes of pregnancies  
exposed to mycophenolate during pregnancy or  
within 6 weeks following discontinuation of treatment.  
The registry will collect data on the following:  
• Pregnancy loss during the first trimester  
• Fetal malformations, such as microtia  
• Other congenital anomalies, including cleft lip and palate  
• Survival of the fetus or infant  
• Birth weight, length, and head circumference  
• Gestational age at birth  
• Date of delivery  
• Date of last menstrual period  
• Date of conception  
• Date of exposure to mycophenolate  
• Date of discontinuation of mycophenolate  
• Date of enrollment in the registry  
• Date of last contact with the registry  
• Date of last follow-up  
• Date of last assessment  
• Date of last visit  
• Date of last contact with the registry  
• Date of last follow-up  
• Date of last assessment  
• Date of last visit

The Mycophenolate Pregnancy Registry will collect data to characterize the risks associated with exposure to mycophenolate during pregnancy or within 6 weeks following discontinuation of treatment, regardless of indication. There is no limit to the number or type of physicians and/or patients who may contribute data to the Mycophenolate Pregnancy Registry. All reports of potential maternal and fetal exposure to mycophenolate will be considered for the Mycophenolate Pregnancy Registry.

The success of the Mycophenolate Pregnancy Registry depends on the participation of both patients and healthcare providers. Healthcare providers should identify patients who are currently pregnant or who may have been exposed to mycophenolate while pregnant, inform them of the Mycophenolate Pregnancy Registry, and encourage them to participate in the Mycophenolate Pregnancy Registry. Healthcare providers should report any pregnancy that may involve exposure to mycophenolate, whether or not the patient chooses to participate. Patients should be informed that you will report any pregnancies of which you become aware to the Mycophenolate Pregnancy Registry.



## Frequently Asked Questions About Mycophenolate REMS and the Mycophenolate Pregnancy Registry (cont'd)

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### What is my role in the Mycophenolate Pregnancy

Instruct patients to tell you if they get pregnant during late or within 6 weeks following discontinuation of treatment. If you learn that a patient is

pregnant, notify the Mycophenolate

Pregnancy Registry. Encourage the patient to participate in the Mycophenolate Pregnancy Registry.

When you inform the patient of her pregnancy to the Mycophenolate Pregnancy Registry, you should provide her with contact information. Also provide the patient with information about the patient's contact information for follow-up for this safety monitoring of patient contact and medical history. Mycophenolate Pregnancy Registry HIPAA waiver.

When the patient is enrolled in the Mycophenolate Pregnancy Registry, they agree to provide information about their pregnancy, including information about the duration of any exposure, maternal history, and maternal and fetal outcomes. The patient agrees to participate in the Mycophenolate Pregnancy Registry as soon as their pregnancy is known, preferably in the first trimester.

### After I report my patient's pregnancy, what will her participation involve?

The patient will be asked in telephone interviews to answer questions regarding her health and her baby's health. These interviews will take place during each trimester of pregnancy; near the expected time of delivery or at pregnancy outcome; and when the infant reaches 2 months, 6 months, and 1 year of age. Since the Mycophenolate Pregnancy Registry relies on being able to contact the patient, it is important for you to advise her to keep the Mycophenolate Pregnancy Registry informed of any changes to her contact information throughout her participation.

### After I enroll my patient, what is my role?

You will be asked to provide pregnancy and outcomes data on a paper-based case report form (CRF) and submit it via mail or fax, or enter the data into an electronic data capture (EDC) system. You must keep the Mycophenolate Pregnancy Registry informed of any changes to your contact information throughout your participation.

## Frequently Asked Questions About Mycophenolate REMS and the Mycophenolate Pregnancy Registry (cont'd)

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### **How can pregnancy data collected by the Mycophenolate Pregnancy Registry program be analyzed and reported?**

Pregnancy data collected by the Mycophenolate Pregnancy Registry program will be personally identifiable. Pregnancy data to the appropriate drug manufacturer for regulatory agencies as required. Anonymized data may be shared with other sponsors of Mycophenolate REMS. Data will be published in peer-reviewed journals.

### **How should pregnancies to the National Transplantation Pregnancy Registry (NTPR) be reported?**

Pregnancies occurring during treatment with Mycophenolate should be reported to the NTPR, regardless of the indication, for inclusion and follow-up. In addition to reporting pregnancies to the Mycophenolate Pregnancy Registry, report pregnancies to the NTPR.

### **How can I obtain more information?**

- Visit [www.MycophenolatePregnancyRegistry.com](http://www.MycophenolatePregnancyRegistry.com)
- Visit [www.MycophenolateREMS.com](http://www.MycophenolateREMS.com)
- Call 1-800-617-8191



## Mycophenolate REMS Resources

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been developed to help ensure prescribers understand the risks associated with mycophenolate during pregnancy and to help you comply with the requirements of Mycophenolate REMS. These resources, some of which have been developed previously, are available either in the English or Spanish version of *View & Your Birth Control Options* booklet.

### **Mycophenolate REMS Web Site:** **[mycophenolateREMS.com](http://mycophenolateREMS.com)**

The website provides information about Mycophenolate REMS, including the option to order or download resources. The *View & Your Birth Control Options* booklet in Mycophenolate REMS can also be completed on this site.

### **Mycophenolate REMS Brochure for Healthcare Providers**

### **Training Confirmation Form**

to enroll in Mycophenolate REMS by

### **Center Training Confirmation Form**

to enroll in Mycophenolate REMS by completing

### **Obstetrician/Gynecologist Referral Template**

Referral letters available online at  
**[mycophenolateREMS.com](http://mycophenolateREMS.com)** can be used by

prescribers of mycophenolate to help establish a working relationship with an OB/GYN for patient counseling. There are 2 letter templates—one for contraception counseling and one for pregnancy planning education—that can be customized for your practice and patient before sending to an OB/GYN.

### ■ **Medication Guide**

There is a separate Medication Guide for each mycophenolate formulation.

### ■ **Mycophenolate REMS Overview & Your Birth Control Options**

This booklet helps patients understand Mycophenolate REMS and gives patients an overview of acceptable forms of contraception. Included in the booklet are

- **Patient-Prescriber Acknowledgment Form**  
HCPs and females of reproductive potential sign this to acknowledge that they have been informed about the risks and will comply with Mycophenolate REMS.
- **Mycophenolate Pregnancy Registry Frequently Asked Questions for Patients**  
This document answers some common questions about the Mycophenolate Pregnancy Registry in patient-friendly language.

## Mycophenolate REMS Resources (cont'd)

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**Mycophenolate Pregnancy Registry**  
The pregnancy Registry evaluates  
exposed pregnancies and their  
outcomes. Contact the Mycophenolate  
Pregnancy Registry by calling **1-800-617-8191** or  
**[cophenolatePregnancyRegistry.com](http://cophenolatePregnancyRegistry.com)**

**For more information about Mycophenolate REMS and for**

**[cophenolateREMS.com](http://cophenolateREMS.com)**

## Additional Resources

### FOR MORE INFORMATION ABOUT CONTRACEPTION\*

■ Association of Reproductive Health Professionals:  
**[www.arhp.org](http://www.arhp.org)**

■ Planned Parenthood: **[www.plannedparenthood.org](http://www.plannedparenthood.org)**

### FOR MORE INFORMATION ABOUT BIRTH DEFECTS\*

■ Centers for Disease Control and Prevention: **[www.cdc.gov](http://www.cdc.gov)**

\*Mycophenolate REMS is neither affiliated with nor an endorser of these organizations. The information provided by Mycophenolate REMS or these organizations is meant for informational purposes only, and is not intended to replace your medical advice to your patients.



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BHCP 11/11

# OVERVIEW & YOUR BIRTH CONTROL OPTIONS BOOKLET



# MYCOPHENOLATE REMS

MYCOPHENOLATE-RELATED RISK OF MISCARRIAGE AND BIRTH DEFECTS

## OVERVIEW & YOUR BIRTH CONTROL OPTIONS

For complete safety information, please see the *Medication Guide*, which can be found at [www.MycophenolateREMS.com](http://www.MycophenolateREMS.com)



OVERVIEW  
FOR PATIENTS

MYCOPHENOLATE REMS

MYCOPHENOLATE-RELATED RISK OF MISCARRIAGE AND BIRTH DEFECTS

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## Mycophenolate REMS

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Females who take mycophenolate and can get pregnant should participate in Mycophenolate REMS (Risk Evaluation and Mitigation Strategy). Mycophenolate REMS has been designed to tell you about the risks of taking mycophenolate.

taking mycophenolate while they are pregnant have a higher risk of miscarriage in the first 3 months. There is also a higher risk that the baby will have birth defects.

ain mycophenolate:

(mycophenolate mofetil)

(mycophenolic acid)

Generic formulations of mycophenolate mofetil

Generic formulations of mycophenolic acid

*Mycophenolate REMS Overview & Your Birth Control Options*, tells you what you need to know about . It explains how it works and what your role is.

Please read all of the information in this booklet. Talk with your doctor if you have questions.

information, please the *Medication Guide*, which can be found at [www.MycophenolateREMS.com](http://www.MycophenolateREMS.com)

## What You Need to Know

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If you are a girl or woman who can get pregnant, talk with your doctor about the risks of mycophenolate during pregnancy. Talk with your doctor about birth control and pregnancy planning.

### **use acceptable birth control**

During your entire treatment with

For 6 weeks after you stop taking

Unless you choose not to have sexual intercourse with a partner (sexual abstinence), you must always use

**It is important to talk with your doctor about the best forms of birth control for you.**

Discuss your options for birth control during treatment with mycophenolate.

### **If you are thinking about having a baby**

- Tell your doctor right away
- Do not stop taking mycophenolate on your own
- In some cases, you and your doctor may decide that your medicine is more important to your health than the possible risks to your unborn baby

If you get pregnant while you are taking mycophenolate or within 6 weeks after you stop, tell your doctor right away.

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If you are a girl or woman who can get pregnant, you should take part in Mycophenolate REMS while you are

about mycophenolate use and risk of miscarriage or birth defects.

*Patient-Prescriber Acknowledgment Form.*

h your doctor what birth control methods

You should have one pregnancy test immediately before starting mycophenolate and another pregnancy test 8 to 10 days later. Pregnancy tests repeated during routine follow-up visits with your doctor. Talk to your doctor about the results of all of your pregnancy tests.

5. If you are thinking about having a baby, talk with your doctor right away.
6. If you get pregnant while you are taking mycophenolate or within 6 weeks after you stop, tell your doctor right away.
7. If you get pregnant while you are taking mycophenolate, participate in the Mycophenolate Pregnancy Registry. The information you provide helps patients and doctors understand the effects of mycophenolate during pregnancy.



## Your Birth Control Options

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ing birth control is very personal. This booklet gives  
th control methods you can use  
while taking mycophenolate. This information should be  
used along with your doctor's medical advice. After you  
read this booklet, talk with your doctor or  
obstetrician/gynecologist. Then you and your doctor  
can decide what is best for you.

### **use acceptable birth control**

During your entire treatment with mycophenolate

For 6 weeks after you stop taking mycophenolate

Unless you choose not to have sexual intercourse with a  
nence), you must always use

**need to use more than one method of birth  
control at the same time.**

**intrauterine device (IUD)**, had

(had your tubes tied or blocked),

or if your partner has had a **vasectomy**, you do not need  
to use a second form of birth control.

### **Mycophenolate could reduce the effectiveness of hormonal methods of birth control.**

- Hormonal methods of birth control must be used  
with a barrier method because studies show that  
mycophenolate decreases blood levels of certain  
hormones in the **oral contraceptive pill**. It is  
possible that mycophenolate could reduce the  
effectiveness of the oral contraceptive pill
- The effectiveness of other hormone methods (like the  
**patch**, the **ring**, the **shot**, and the **implant**) may also  
be reduced while you are taking mycophenolate

The table on page 7 lists your options for birth control  
during treatment with mycophenolate.

## Your Birth Control Options (cont'd)

The table below lists your options for birth control during treatment with mycophenolate. Pick from the following birth control options:

Acceptable Contraception Methods			
Option 1	<ul style="list-style-type: none"><li>Intrauterine devices (IUDs)</li><li>Tubal sterilization</li><li>Patient's partner had a vasectomy</li></ul>		
Methods to Use Alone			
OR			
Option 2	Hormone Methods choose 1		Barrier Methods choose 1
Choose One Hormone Method AND One Barrier Method	<b>Estrogen and Progesterone</b> <ul style="list-style-type: none"><li>Oral contraceptive pill</li><li>Transdermal patch</li><li>Vaginal ring</li></ul> <b>Progesterone-only</b> <ul style="list-style-type: none"><li>Injection</li><li>Implant</li></ul>	AND	<ul style="list-style-type: none"><li>Diaphragm with spermicide</li><li>Cervical cap with spermicide</li><li>Contraceptive sponge</li><li>Male condom</li><li>Female condom</li></ul>
OR			
Option 3	Barrier Methods choose 1		Barrier Methods choose 1
Choose One Barrier Method From Each Column ( <i>must choose two methods</i> )	<ul style="list-style-type: none"><li>Diaphragm with spermicide</li><li>Cervical cap with spermicide</li><li>Contraceptive sponge</li></ul>	AND	<ul style="list-style-type: none"><li>Male condom</li><li>Female condom</li></ul>

egnancy

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If you get pregnant while taking mycophenolate or within 6 weeks after you stop, call your doctor right away. Do not stop taking your mycophenolate. Your doctor will talk with you about taking part in the Mycophenolate Pregnancy Registry.

Your doctor should report pregnancies to the Registry. If you would like to report a pregnancy to the Registry

and choose  
“Mycophenolate Pregnancy Registry”

[mycophenolatePregnancyRegistry.com](http://mycophenolatePregnancyRegistry.com)

There are many resources to help you get the information you need about Mycophenolate REMS.

***Mycophenolate REMS Overview & Your Birth  
Defects booklet***

***Patient-Prescriber Acknowledgment Form***

After a discussion with your doctor about mycophenolate use and risk of miscarriage or birth defects, both of you will sign this form. It is included

**Medication Guide for mycophenolate**

Gives you important safety information you need to know about your medicine

■ **Mycophenolate REMS Web site:  
[www.MycophenolateREMS.com](http://www.MycophenolateREMS.com)**

Provides access to all Mycophenolate REMS resources and materials.

■ **Mycophenolate Pregnancy Registry**

Collects information about pregnancies that occur during treatment with mycophenolate or within 6 weeks after stopping. You can contact the Registry by calling **1-800-617-8191** or by visiting **[www.MycophenolatePregnancyRegistry.com](http://www.MycophenolatePregnancyRegistry.com)**

■ ***Mycophenolate Pregnancy Registry Frequently Asked Questions for Patients***

Provides answers to frequently asked questions about the Registry. You can obtain this from your healthcare provider or by visiting: **[www.MycophenolateREMS.com](http://www.MycophenolateREMS.com)**



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**For more information about birth control\***

Association of Reproductive Health Professionals:

**[www.plannedparenthood.org](http://www.plannedparenthood.org)**

**birth control\***

your doctor or pharmacy

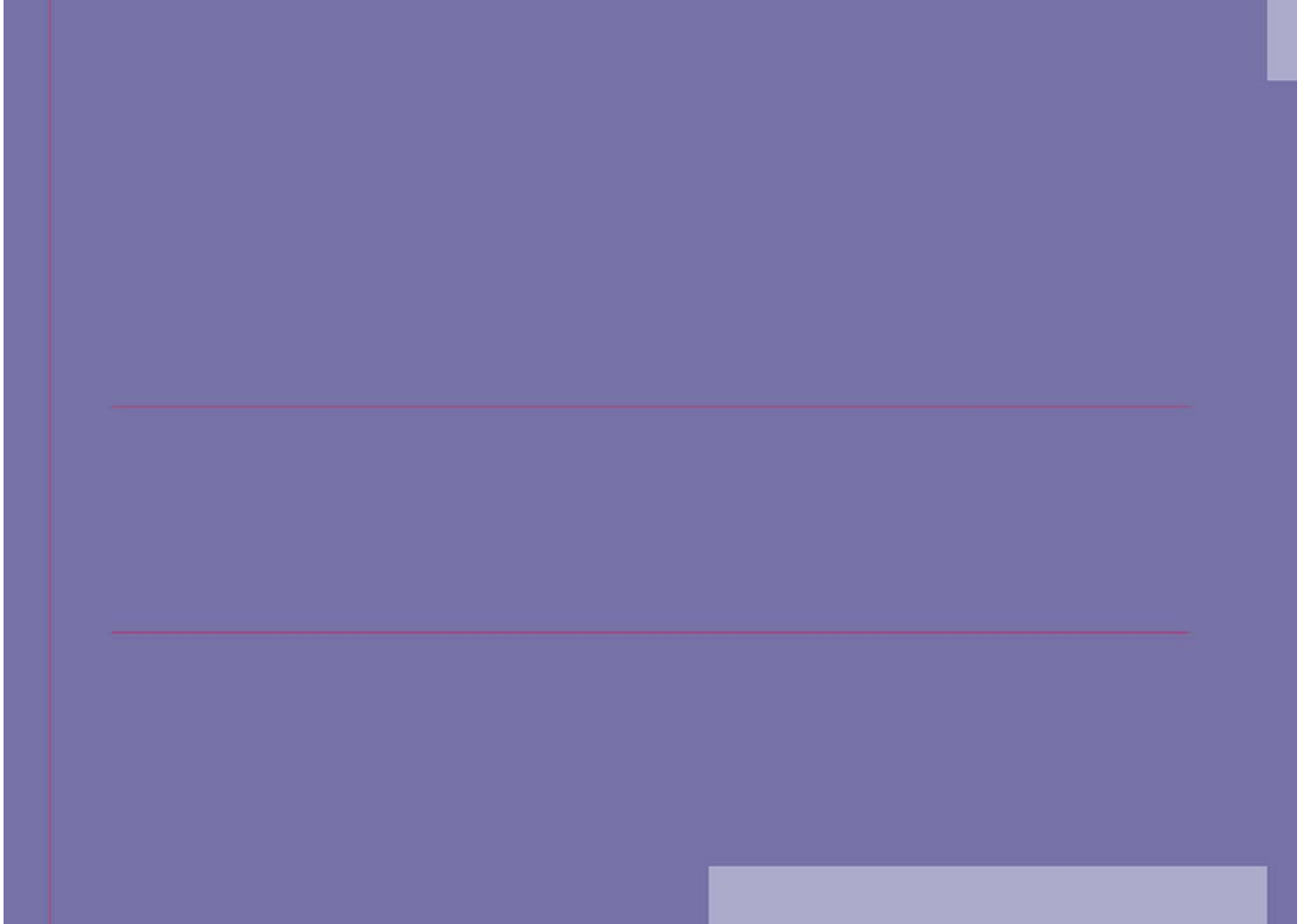
Contraception Hotline:

**1-888-NOT-2-LATE (1-888-668-2528)**

neither affiliated with nor  
nizations. The information  
te REMS or these  
formational purposes  
t intended to replace your doctor's

**For more information about Mycophenolate REMS**

- Read the ***Mycophenolate REMS Overview & Your Birth Control Options*** (this booklet)
- Talk with your doctor
- Visit the Mycophenolate REMS Web site:  
**[www.MycophenolateREMS.com](http://www.MycophenolateREMS.com)**
- Call **1-800-617-8191**





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# FREQUENTLY ASKED QUESTIONS FOR PATIENTS

## MYCOPHENOLATE PREGNANCY REGISTRY FREQUENTLY ASKED QUESTIONS FOR PATIENTS

### **What is the Mycophenolate Pregnancy Registry?**

The Registry collects information about pregnancies that occur during treatment with mycophenolate or within 6 weeks after stopping.

### **Why should I take part in the Mycophenolate Pregnancy Registry?**

The information you provide to the Registry will help us better understand the effects of mycophenolate in pregnancy.

When you take part in the Registry, you provide important information that may help you and other women who take mycophenolate during their pregnancies. Women taking mycophenolate while they are pregnant have a higher risk of miscarriage in the first 3 months. There is also a higher risk that the baby will have birth defects.

### **Who can be in the Mycophenolate Pregnancy Registry?**

1. All females who get pregnant while taking mycophenolate and
2. All females who get pregnant within 6 weeks after stopping treatment with mycophenolate

These medicines contain mycophenolate:

- CellCept® (mycophenolate mofetil)
- Myfortic® (mycophenolic acid)
- Generic formulations of mycophenolate mofetil
- Generic formulations of mycophenolic acid

Tell your doctor right away if you get pregnant. Your doctor will report your pregnancy to the Registry. We encourage you to take part in the Registry. The information you provide to the Registry will help us better understand the effects of mycophenolate in pregnancy. All the information you provide will be kept private.

### **What will I need to do to take part in the Mycophenolate Pregnancy Registry?**

There are a few simple steps to take.

#### **1. Tell your doctor if you get pregnant**

The Registry will contact you after speaking with your doctor.

**(Turn page)**

For complete safety information, please see the *Medication Guide* which can be found at [www.MycophenolateREMS.com](http://www.MycophenolateREMS.com)

## **2. Complete an *Informed Consent* form**

- The *Informed Consent* form will be mailed to you
- The form tells you what to expect with the Registry. It tells you what your rights are
- By signing, you allow the Registry to ask you questions about your health and your baby's health. The Registry will also ask for information from your doctors

## **3. Answer the Registry's questions about your health and your baby's health**

- After the first 3 months of pregnancy
- 2 more times during the next 6 months of pregnancy
- At the time of expected delivery
- When your baby is 2 months, 6 months and 1 year

## **4. Let the Registry know if your contact information changes**

- The Registry relies on your information to contact you. If your contact information changes, please call **1-800-617-8191**

## **What are my rights if I take part in the Mycophenolate Pregnancy Registry?**

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1. You can quit at any time
2. Your privacy is protected

## **What if I do not want to take part in the Mycophenolate Pregnancy Registry?**

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You only take part in the Registry if you want to do it. If you decide not to participate, it will not change your medical care.

## **How can I get more information?**

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- Call **1-800-617-8191** and choose "Mycophenolate Pregnancy Registry" from the menu
- Visit **[www.MycophenolatePregnancyRegistry.com](http://www.MycophenolatePregnancyRegistry.com)**
- For more information about Mycophenolate REMS, visit **[www.MycophenolateREMS.com](http://www.MycophenolateREMS.com)**

# PATIENT-PRESCRIBER ACKNOWLEDGMENT FORM

## PATIENT-PRESCRIBER ACKNOWLEDGMENT FORM

### These medicines contain mycophenolate:

- CellCept® (mycophenolate mofetil)
- Myfortic® (mycophenolic acid)
- Generic formulations of mycophenolate mofetil
- Generic formulations of mycophenolic acid

### For the patient:

Please read each item below. Discuss them with your doctor. Do not sign this form until you are sure you understand it.

By signing on the next page, I am stating that

1. My doctor gave me the *Mycophenolate REMS Overview & Your Birth Control Options* booklet.
2. I know the risks to an unborn baby if I take mycophenolate while I am pregnant. I talked with my doctor about these risks. I understand that if I get pregnant while taking mycophenolate or within 6 weeks after I stop, there is
  - A higher risk of losing the pregnancy (miscarriage) in the first 3 months
  - A higher risk that the baby will have birth defects.
3. I know I will have pregnancy tests before I start and during my mycophenolate treatment
4. My doctor talked with me about acceptable forms of birth control.
5. Unless I choose not to have sexual intercourse with a man at any time (abstinence), I will always use acceptable birth control
  - During my entire treatment with mycophenolate
  - For 6 weeks after I stop taking mycophenolate

**Information about your birth control options is provided in the *Mycophenolate REMS Overview & Your Birth Control Options* booklet.**

6. If I am thinking about having a baby during my treatment, I will talk with my doctor right away.
7. I will tell my doctor right away if I get pregnant during my treatment or within 6 weeks after I stop.
8. I know that my doctor will report any pregnancies to the Mycophenolate Pregnancy Registry.

**(Please fill out form on next page)**

**For complete safety information, please see full *Prescribing Information*, including Boxed WARNING and Medication Guide, which can be found at [www.MycophenolateREMS.com](http://www.MycophenolateREMS.com)**



## **PATIENT-PRESCRIBER ACKNOWLEDGMENT FORM**

Patient Name (please print): \_\_\_\_\_

Patient Signature: \_\_\_\_\_ Date: \_\_\_\_\_

Parent/Guardian Name (if patient under age 18; please print): \_\_\_\_\_

Parent/Guardian Signature: \_\_\_\_\_ Date: \_\_\_\_\_

### **For the prescriber (or healthcare provider acting on behalf of the prescriber):**

I have fully explained to my patient (and her parent or guardian if the patient is under age 18) the nature and purpose of treatment with mycophenolate and the risks to females of reproductive potential as described on the previous page. I have asked the patient (and her parent or guardian) if she has any questions regarding her treatment and have answered those questions to the best of my ability.

Prescriber's/Other Healthcare Provider's Name (please print): \_\_\_\_\_

Degree: (Circle one) MD DO NP PA

Prescriber's/Other Healthcare Provider's Signature: \_\_\_\_\_

Date: \_\_\_\_\_

**PLEASE RETAIN THE ORIGINAL SIGNED DOCUMENT  
AND PROVIDE A COPY TO THE PATIENT.**

For more information about Mycophenolate REMS and to request resource materials, please visit **[www.MycophenolateREMS.com](http://www.MycophenolateREMS.com)** or call **1-800-617-8191**.

# PRESCRIBER TRAINING CONFIRMATION FORM



## PREScriBER TRAINING CONFIRMATION FORM

The FDA determined that a REMS (Risk Evaluation and Mitigation Strategy) is necessary to ensure that the benefits of mycophenolate outweigh the risks of first trimester pregnancy loss and congenital malformations associated with mycophenolate use during pregnancy.

Mycophenolate is available by prescription as

- CellCept® (mycophenolate mofetil)
- Myfortic® (mycophenolic acid)
- Generic formulations of mycophenolate mofetil
- Generic formulations of mycophenolic acid

As a prescriber of mycophenolate to females of reproductive potential\*, I understand that I need to complete and return the *Training Confirmation Form* to enroll in Mycophenolate REMS.

\*A female of reproductive potential includes girls who have entered puberty and all females who have a uterus and have not passed through menopause.

I agree to do the following:

1. Read and understand the full *Prescribing Information* for mycophenolate and the *Mycophenolate REMS Brochure for Healthcare Providers*.
2. Understand the risks of first trimester pregnancy loss and congenital malformations associated with mycophenolate.
3. Educate females of reproductive potential on the risks associated with exposure to mycophenolate during pregnancy.
4. Provide a *Mycophenolate REMS Overview & Your Birth Control Options* booklet to females of reproductive potential.
5. Provide contraception counseling to patients directly or by partnering with an OB/GYN.
6. Only prescribe mycophenolate to a pregnant patient if the benefits of initiating or continuing treatment outweigh the risk of fetal harm.
7. Discuss alternative treatments to mycophenolate with females of reproductive potential who are pregnant or considering pregnancy.
8. Follow the pregnancy testing recommendations as outlined in the full *Prescribing Information* for mycophenolate and the *Mycophenolate REMS Brochure for Healthcare Providers*.
9. Report to the Mycophenolate Pregnancy Registry any pregnancies that occur during mycophenolate treatment or within 6 weeks following discontinuation of treatment. Encourage pregnant patients to participate in the Mycophenolate Pregnancy Registry.
10. Obtain a signed *Patient-Prescriber Acknowledgment Form* from each female of reproductive potential.

I understand that I may be contacted in the future for items pertaining to the administration of Mycophenolate REMS.

(PLEASE PRINT)

Complete all fields below:

Prescriber  
First Name: \_\_\_\_\_ Prescriber  
Last Name: \_\_\_\_\_

Prescriber Degree: MD, DO, NP, PA (Circle One)

Specialty Code (*Select one from the back of this form*) \_\_\_\_\_ National Provider Identifier: \_\_\_\_\_

Prescriber E-mail Address: \_\_\_\_\_

Facility: \_\_\_\_\_

Address 1: \_\_\_\_\_

Address 2: \_\_\_\_\_

City: \_\_\_\_\_ State: \_\_\_\_\_ ZIP: \_\_\_\_\_

Telephone: \_\_\_\_\_ Fax: \_\_\_\_\_

Prescriber Signature: \_\_\_\_\_ Date: \_\_\_\_\_

Healthcare Provider acting on behalf of the prescriber: \_\_\_\_\_

Degree: RN, LPN, NP, PA, RPH, PharmD, CSW (Circle One)

**For complete safety information, please see full Prescribing Information, including Boxed WARNING and Medication Guide, which can be found at [www.MycophenolateREMS.com](http://www.MycophenolateREMS.com)**



## PRESCRIBER TRAINING CONFIRMATION FORM

You can submit a *Prescriber Training Confirmation Form* by visiting **www.MycophenolateREMS.com** and completing the online form.

If you prefer, you can complete the paper form and return it via fax to 1-800-617-5768 or mail it to:

Mycophenolate REMS  
200 Pinecrest Plaza  
Morgantown, WV 26505-8065

You can also call **1-800-617-8191** to complete a *Prescriber Training Confirmation Form*.

For more information about Mycophenolate REMS, visit **www. MycophenolateREMS.com** or call **1-800-617-8191**.

Specialty	Specialty Code
Allergy and Immunology .....	1
Cardiology .....	2
Dermatology .....	3
Family Practitioner .....	4
Gastroenterology .....	5
Hepatology .....	6
Internal Medicine .....	7
Nephrology .....	8
Neurology .....	9
OB/GYN .....	10
Pediatric .....	11
Rheumatology .....	12
Surgery .....	13
Transplant .....	14
Other .....	15

# CENTER TRAINING CONFIRMATION FORM

## CENTER TRAINING CONFIRMATION FORM

The FDA determined that a REMS (Risk Evaluation and Mitigation Strategy) is necessary to ensure that the benefits of mycophenolate outweigh the risks of first trimester pregnancy loss and congenital malformations associated with mycophenolate use during pregnancy.

Mycophenolate is available by prescription as:

- CellCept® (mycophenolate mofetil)
- Myfortic® (mycophenolic acid)
- Generic formulations of mycophenolate mofetil
- Generic formulations of mycophenolic acid

On behalf of prescribers of mycophenolate to females of reproductive potential,\* (place center name here) will complete and return this training form to enroll in Mycophenolate REMS.

\*A female of reproductive potential includes girls who have entered puberty and all women who have a uterus and have not passed through menopause.

We agree to do the following:

1. Read and understand the full *Prescribing Information* for mycophenolate and the *Mycophenolate REMS Brochure for Healthcare Providers*
2. Understand the risks of first trimester pregnancy loss and congenital malformations associated with mycophenolate.
3. Educate females of reproductive potential on the risks associated with exposure to mycophenolate during pregnancy.
4. Provide a *Mycophenolate REMS Overview & Your Birth Control Options* booklet to females of reproductive potential.
5. Provide contraception counseling to patients directly or by partnering with an OB/GYN.
6. Only prescribe mycophenolate to a pregnant patient if the benefits of initiating or continuing treatment outweigh the risk of fetal harm.
7. Discuss alternative treatments to mycophenolate with females of reproductive potential who are pregnant or considering pregnancy.
8. Follow the pregnancy testing recommendations as outlined in the full *Prescribing Information* for mycophenolate and the *Mycophenolate REMS Brochure for Healthcare Providers*.
9. Report to the Mycophenolate Pregnancy Registry any pregnancies that occur during mycophenolate treatment or within 6 weeks following discontinuation of treatment. Encourage pregnant patients to participate in the Mycophenolate Pregnancy Registry.
10. Obtain a signed *Patient-Prescriber Acknowledgment Form* from each female of reproductive potential.
11. Describe how your center plans to implement the program requirements (please explain/outline process below):

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I understand that I may be contacted in the future for items pertaining to the administration of Mycophenolate REMS.

(Please fill out form on next page)

**For complete safety information, please see full *Prescribing Information*, including Boxed WARNING and *Medication Guide*, which can be found at [www.MycophenolateREMS.com](http://www.MycophenolateREMS.com)**



**MYCOPHENOLATE REMS**  
RISKS OF FIRST TRIMESTER PREGNANCY LOSS AND CONGENITAL MALFORMATIONS

## CENTER TRAINING CONFIRMATION FORM

### CENTER INFORMATION

(PLEASE PRINT)

Center: \_\_\_\_\_

Center Type (disease or specialty)\* \_\_\_\_\_

Address: \_\_\_\_\_

City: \_\_\_\_\_ State: \_\_\_\_\_ ZIP: \_\_\_\_\_

Phone: \_\_\_\_\_ Fax: \_\_\_\_\_

Contact Person: \_\_\_\_\_ Email: \_\_\_\_\_

### TRAINED PRESCRIBERS

Please complete fields below:

Prescriber Name (Printed)	Signature of Prescriber	Date	Degree (MD, DO, NP, PA)	Specialty Code(s)*	Email	National Provider Identifier (NPI)

\*A list of specialty codes can be found on page 4.

■ Healthcare providers acting on behalf of the prescriber should fill out the form on the next page (Please fill out form

(Please fill out form on next page)

## CENTER TRAINING CONFIRMATION FORM

### HEALTHCARE PROVIDERS ACTING ON BEHALF OF THE PRESCRIBER

Please complete fields below:

Provider Name (Printed)	Signature of Provider	Date	Degree (RN, LPN, NP, PA, RPH, PharmD, CSW)	Specialty Code(s)*	Email	Name of Prescriber you are signing for

\*A list of specialty codes can be found on page 4.

(Turn page)



## CENTER TRAINING CONFIRMATION FORM

You can submit a completed *Center Training Confirmation Form* via fax to 1-800-617-5768 or mail it to:

Mycophenolate REMS  
200 Pinecrest Plaza  
Morgantown, WV 26505-8065

For more information about Mycophenolate REMS, visit [www.MycophenolateREMS.com](http://www.MycophenolateREMS.com) or call 1-800-617-8191.

Specialty	Specialty Code
Allergy and Immunology .....	1
Cardiology .....	2
Dermatology .....	3
Family Practitioner .....	4
Gastroenterology .....	5
Hepatology .....	6
Internal Medicine .....	7
Nephrology .....	8
Neurology .....	9
OB/GYN .....	10
Pediatric .....	11
Rheumatology .....	12
Surgery .....	13
Transplant .....	14
Other .....	15

Center Type	Center Type Code
Allergy and Immunology .....	1
Cardiology .....	2
Dermatology .....	3
Dermatology Surgery .....	4
Dermatopathology .....	5
Gastroenterology .....	6
General Surgery .....	7
Hepatology .....	8
Immunology .....	9
Maternal Fetal Medicine .....	10
Nephrology .....	11
Neurologic Surgery .....	12
Neurology .....	13
Neuropathology .....	14
OB/GYN .....	15
Rheumatology .....	16
Thoracic Surgery .....	17
Transplantation Surgery .....	18

# DEAR HEALTHCARE PROVIDER LETTER



## IMPORTANT DRUG WARNING

Regarding Mycophenolate-Containing Products

Dear Healthcare Provider:

Mycophenolate REMS (Risk Evaluation and Mitigation Strategy) has been mandated by the FDA (Food and Drug Administration) due to postmarketing reports showing that exposure to mycophenolate during pregnancy is associated with increased risks of first trimester pregnancy loss and congenital malformations.

Mycophenolate is available by prescription as

- CellCept® (mycophenolate mofetil)
- Myfortic® (mycophenolic acid)
- Generic formulations of mycophenolate mofetil
- Generic formulations of mycophenolic acid

The goals of the Mycophenolate REMS are:

1. To prevent unplanned pregnancy in patients using mycophenolate and to minimize fetal exposure to mycophenolate by informing prescribers and females of reproductive potential about
  - the increased risks of first trimester pregnancy loss and congenital malformations associated with exposure to mycophenolate during pregnancy; and
  - the importance of pregnancy prevention and planning
2. To minimize the risks associated with fetal exposure to mycophenolate by collecting information on pregnancy outcomes through the Mycophenolate Pregnancy Registry
3. To inform patients about the serious risks associated with mycophenolate

### What you need to know to prescribe mycophenolate

All prescribers of mycophenolate and females of reproductive potential,\* whether or not they plan to get pregnant, should participate in Mycophenolate REMS. If you prescribe mycophenolate to females of reproductive potential (new and continuing patients), **you should receive training and agree to do the following:**

- Understand the risks of first trimester pregnancy loss and congenital malformations associated with mycophenolate
- Educate females of reproductive potential on the risks associated with exposure to mycophenolate during pregnancy
- Provide a *Mycophenolate REMS Overview & Your Birth Control Options* booklet to females of reproductive potential
- Provide contraception counseling to patients directly or by partnering with an OB/GYN
- Only prescribe mycophenolate to a pregnant patient if the benefits of initiating or continuing treatment outweigh the risk of fetal harm
- Discuss alternative treatments to mycophenolate with females of reproductive potential who are pregnant or considering pregnancy
- Follow the pregnancy testing recommendations

\*A female of reproductive potential includes girls who have entered puberty and all women who have a uterus and have not yet passed through menopause.

**(Continued on next page)**

**For complete safety information, please see full *Prescribing Information*, including Boxed WARNING and *Medication Guide*, which can be found at [www.MycophenolateREMS.com](http://www.MycophenolateREMS.com)**

## IMPORTANT DRUG WARNING

Regarding Mycophenolate-Containing Products



- Report to the Mycophenolate Pregnancy Registry any pregnancies that occur during mycophenolate treatment or within 6 weeks following discontinuation of treatment. Encourage pregnant patients to participate in the Mycophenolate Pregnancy Registry
- Obtain a signed *Patient-Prescriber Acknowledgement Form* from females of reproductive potential

Please note that the manufacturers may contact you in the future for assessment of Mycophenolate REMS.

This letter is not a comprehensive description of the risks associated with the use of mycophenolate. **For complete safety information, please see full *Prescribing Information*, including Boxed WARNING and Medication Guide, which can be found at [www.MycophenolateREMS.com](http://www.MycophenolateREMS.com).**

For more information about Mycophenolate REMS, including all program materials and instructions on how to enroll, please visit **[www.MycophenolateREMS.com](http://www.MycophenolateREMS.com)** or call **1-800-617-8191**.

The FDA requests healthcare providers report any pregnancies of which they become aware. Pregnancies that occur during treatment with mycophenolate or within 6 weeks following discontinuation of treatment should be reported by contacting the Mycophenolate Pregnancy Registry.

- By phone: **1-800-617-8191**
- Online: **[www.MycophenolatePregnancyRegistry.com](http://www.MycophenolatePregnancyRegistry.com)**
- Or by mail: Mycophenolate Pregnancy Registry  
201 Broadway, Suite 5  
Cambridge, MA 02139

Thank you for your commitment to helping patients understand the risks and benefits associated with mycophenolate treatment.

Sincerely,

Mycophenolate REMS Team

(Continued on next page)



## IMPORTANT DRUG WARNING

Regarding Mycophenolate-Containing Products

### Indications and Important Selected Safety Information About Mycophenolate-Containing Products

#### INDICATIONS:

**CellCept® (mycophenolate mofetil)** is indicated for the prophylaxis of organ rejection in patients receiving allogeneic renal, cardiac or hepatic transplants. CellCept should be used concomitantly with cyclosporine and corticosteroids.

**Myfortic® (mycophenolic acid)** is indicated for the prophylaxis of organ rejection in patients receiving allogeneic renal transplants, administered in combination with cyclosporine and corticosteroids.

**Mycophenolate mofetil** is indicated for the prophylaxis of organ rejection in patients receiving allogeneic renal, cardiac or hepatic transplants. Mycophenolate mofetil should be used concomitantly with cyclosporine and corticosteroids.

**Mycophenolic acid** is indicated for the prophylaxis of organ rejection in patients receiving allogeneic renal transplants, administered in combination with cyclosporine and corticosteroids.

#### CONTRAINDICATIONS:

- Allergic reactions to mycophenolate-containing products have been observed; therefore, mycophenolate-containing products are contraindicated in patients with a hypersensitivity to mycophenolate mofetil, mycophenolic acid or any component of the drug product.
- CellCept Intravenous is contraindicated in patients who are allergic to Polysorbate 80 (TWEEN)

#### **WARNING: EMBRYOFETAL TOXICITY, MALIGNANCIES AND SERIOUS INFECTIONS**

**Use during pregnancy is associated with increased risks of first trimester pregnancy loss and congenital malformations. Females of reproductive potential (FRP) must be counseled regarding pregnancy prevention and planning.**

**Immunosuppression may lead to increased susceptibility to infection and possible development of lymphoma and other neoplasms. Only physicians experienced in immunosuppressive therapy and management of organ transplant recipients should prescribe mycophenolate-containing products. Patients receiving mycophenolate-containing products should be managed in facilities equipped and staffed with adequate laboratory and supportive medical resources. The physician responsible for maintenance therapy should have complete information requisite for the follow-up of the patient.**

(Continued on next page)



**Important Selected Safety Information About Mycophenolate-Containing Products (cont'd)**

**WARNINGS:**

**Embryofetal Toxicity**

- Mycophenolate-containing products can cause fetal harm when administered to a pregnant female. Use of mycophenolate-containing products during pregnancy is associated with an increased risk of first trimester pregnancy loss and an increased risk of congenital malformations, especially external ear and other facial abnormalities including cleft lip and palate, and anomalies of the distal limbs, heart, esophagus, and kidney.

**Pregnancy Exposure Prevention and Planning**

- Females of reproductive potential must be made aware of the increased risk of first trimester pregnancy loss and congenital malformations and must be counseled regarding pregnancy prevention and planning.

**Lymphoma and Malignancy**

- Patients receiving immunosuppressive regimens involving combinations of drugs, including mycophenolate-containing products, as part of an immunosuppressive regimen are at increased risk of developing lymphomas and other malignancies, particularly of the skin.

**Combination with Other Immunosuppressive Agents**

- Mycophenolate mofetil has been administered in combination with the following agents in clinical trials: antithymocyte globulin, OKT3, cyclosporine, and corticosteroids.
- Mycophenolic acid has been administered in combination with the following agents in clinical trials: antithymocyte/lymphocyte immunoglobulin, muromonab-CD3, basiliximab, daclizumab, cyclosporine, and corticosteroids.
- The efficacy and safety of the use of mycophenolate-containing products, in combination with other immunosuppressive agents have not been determined.

**Serious Infections**

- Patients receiving immunosuppressants, including mycophenolate, are at increased risk of developing bacterial, fungal, protozoal and new or reactivated viral infections, including opportunistic infections. These infections may lead to serious, including fatal outcomes.
- Polyomavirus associated nephropathy (PVAN), JC virus associated progressive multifocal leukoencephalopathy (PML), cytomegalovirus (CMV) infections, reactivation of hepatitis B (HBV) or hepatitis C (HCV) have been reported.

**Neutropenia**

- Severe neutropenia [absolute neutrophil count (ANC)  $<0.5 \times 10^3/\mu\text{L}$ ] developed in up to 2.0% of renal, up to 2.8% of cardiac, and up to 3.6% of hepatic transplant patients receiving mycophenolate mofetil 3g daily.
- Patients receiving mycophenolate-containing products should be monitored for neutropenia.
- If neutropenia develops [absolute neutrophil count (ANC)  $<1.3 \times 10^3/\mu\text{L}$ ] or anemia occurs, dosing with mycophenolate-containing products should be interrupted or the dose reduced, appropriate diagnostic tests performed, and the patient managed appropriately.

**Pure Red Cell Aplasia**

- Cases of pure red cell aplasia (PRCA) have been reported in patients treated with mycophenolate-containing products in combination with other immunosuppressive agents. Patients receiving mycophenolate-containing products should be monitored for blood dyscrasias.

**CAUTION: CELLCEPT INTRAVENOUS SOLUTION SHOULD NEVER BE ADMINISTERED BY RAPID OR BOLUS INTRAVENOUS INJECTION**

**(Continued on next page)**



## IMPORTANT DRUG WARNING

Regarding Mycophenolate-Containing Products

### Important Selected Safety Information About Mycophenolate-Containing Products (cont'd)

#### PRECAUTIONS:

##### Pregnancy Exposure Prevention and Planning

- Females of reproductive potential\* must be made aware of the increased risk of first trimester pregnancy loss and congenital malformations and must be counseled regarding pregnancy prevention and planning.
- Females of reproductive potential taking mycophenolate-containing products must receive contraceptive counseling and use acceptable contraception during entire therapy with mycophenolate-containing products and for 6 weeks after stopping therapy (see Full Prescribing Information for acceptable contraception methods).
- Patients should be aware that mycophenolate-containing products reduce blood levels of the hormones in the oral contraceptive pill and could theoretically reduce its effectiveness.
- To prevent unplanned exposure during pregnancy, females of reproductive potential should have a serum or urine pregnancy test with a sensitivity of at least 25 mIU/mL immediately before starting a mycophenolate-containing product.
- Another pregnancy test with the same sensitivity should be done 8 to 10 days later. Repeat pregnancy tests should be performed during routine follow-up visits.
- Results of all pregnancy tests should be discussed with the patient.
- In the event of a positive pregnancy test, females should be counseled with regard to whether the maternal benefits of mycophenolate treatment may outweigh the risks to the fetus in certain situations.
- For patients who are considering pregnancy, consider alternative immunosuppressants with less potential for embryofetal toxicity.

##### Pregnancy Category D

- Mycophenolate-containing products can cause fetal harm when administered to a pregnant female. If mycophenolate-containing products are used during pregnancy, or if the patient becomes pregnant while taking mycophenolate-containing products, the patient should be apprised of the potential hazard to the fetus. In certain situations, the patient and her healthcare practitioner may decide that the maternal benefits outweigh the risks to the fetus. Risks and benefits of mycophenolate-containing products should be discussed with the patient.
- For those females using mycophenolate-containing products at any time during pregnancy and those becoming pregnant within 6 weeks of discontinuing therapy, the healthcare practitioner should report the pregnancy to the **Mycophenolate Pregnancy Registry (1-800-617-8191)**. The healthcare practitioner should also strongly encourage the patient to enroll in the pregnancy registry.

##### Gastrointestinal Disorders

- Gastrointestinal bleeding (requiring hospitalization) has been reported in de novo renal transplant patients (1.0%) and maintenance patients (1.3%) treated with mycophenolic acid (up to 12 months); and in approximately 3% of renal, in 1.7% of cardiac and in 5.4% of hepatic transplant patients treated with mycophenolate mofetil 3g daily.
- Mycophenolate-containing products should be administered with caution in patients with active serious digestive system disease because mycophenolate-containing products have been associated with an increased incidence of digestive system adverse events.

## Important Selected Safety Information About Mycophenolate-Containing Products (cont'd)

### Concomitant Medications

- It is recommended that mycophenolate-containing products not be administered concomitantly with azathioprine because of the potential to cause bone marrow suppression and inhibit purine metabolism.
- Caution should be used in the concomitant administration of mycophenolate-containing products with drugs that interfere with enterohepatic recirculation such as cholestyramine because of the potential to reduce the efficacy of mycophenolate-containing products.

### Immunizations

- During treatment with mycophenolate-containing products, avoid the use of live attenuated vaccines and advise patients that vaccinations may be less effective.

### Phenylketonurics

- Care should be taken if mycophenolate mofetil oral suspension is administered to patients with phenylketonuria. Complete blood counts should be performed weekly during the first month, twice monthly for the second and third months of treatment, then monthly through the first year.

### Nursing Mothers

- It is not known whether mycophenolate-containing products are excreted in human milk. Because many drugs are excreted in human milk, and because of the potential for serious adverse reactions in nursing infants from mycophenolate-containing products, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.
- Patients should not breastfeed during mycophenolate-containing products therapy.

\* A female of reproductive potential includes girls who have entered puberty and all women who have a uterus and have not yet passed through menopause.

### ADVERSE REACTIONS:

- The principal adverse reactions associated with the administration of mycophenolate mofetil include diarrhea, leukopenia, sepsis, vomiting, and there is evidence of a higher frequency of certain types of infections, eg, opportunistic infections. Phlebitis and thrombosis have been reported with intravenous administration.
- The principal adverse reactions associated with the administration of mycophenolic acid include constipation, nausea, and urinary tract infection in de novo patients and nausea, diarrhea, and nasopharyngitis in maintenance patients.

**For additional safety information, please see full Prescribing Information, including Boxed WARNING and Medication Guide, which can be found at [www.MycophenolateREMS.com](http://www.MycophenolateREMS.com)**

# DEAR CENTER DIRECTOR LETTER



Dear Center Director:

Mycophenolate REMS (Risk Evaluation and Mitigation Strategy) has been mandated by the FDA (Food and Drug Administration) due to postmarketing reports showing that exposure to mycophenolate during pregnancy is associated with increased risks of first trimester pregnancy loss and congenital malformations.

Mycophenolate is available by prescription as

- CellCept® (mycophenolate mofetil)
- Myfortic® (mycophenolic acid)
- Generic formulations of mycophenolate mofetil
- Generic formulations of mycophenolic acid

The goals of the Mycophenolate REMS are:

1. To prevent unplanned pregnancy in patients using mycophenolate and to minimize fetal exposure to mycophenolate by informing prescribers and females of reproductive potential about:
  - the increased risks of first trimester pregnancy loss and congenital malformations associated with exposure to mycophenolate during pregnancy; and
  - the importance of pregnancy prevention and planning
2. To minimize the risks associated with fetal exposure to mycophenolate by collecting information on pregnancy outcomes through the Mycophenolate Pregnancy Registry
3. To inform patients about the serious risks associated with mycophenolate

#### Why are you receiving this letter?

To facilitate training about this risk, you can set up training at your center and enroll all healthcare providers who participate. After completing the training, all healthcare providers should read and sign the *Center Training Confirmation Form* sent with this letter.

#### What you need to know to prescribe mycophenolate

All prescribers of mycophenolate and females of reproductive potential,\* whether or not they plan to get pregnant, should participate in Mycophenolate REMS. Healthcare providers who prescribe mycophenolate to females of reproductive potential (new and continuing patients) **should receive training and agree to do the following:**

- Understand the risks of first trimester pregnancy loss and congenital malformations associated with mycophenolate
  - Educate females of reproductive potential on the risks associated with exposure to mycophenolate during pregnancy
  - Provide a *Mycophenolate REMS Overview & Your Birth Control Options* booklet to females of reproductive potential
  - Provide contraception counseling to patients directly or by partnering with an OB/GYN
  - Only prescribe mycophenolate to a pregnant patient if the benefits of initiating or continuing treatment outweigh the risk of fetal harm
  - Discuss alternative treatments to mycophenolate with females of reproductive potential who are pregnant or considering pregnancy
  - Follow the pregnancy testing recommendations
- \* A female of reproductive potential includes girls who have entered puberty and all women who have a uterus and have not passed through menopause.

(Continued on next page)

For complete safety information, please see full *Prescribing Information*, including Boxed WARNING and *Medication Guide*, which can be found at [www.MycophenolateREMS.com](http://www.MycophenolateREMS.com)



**IMPORTANT DRUG WARNING**  
Regarding Mycophenolate-Containing Products

- Report to the Mycophenolate Pregnancy Registry any pregnancies that occur during mycophenolate treatment with or within 6 weeks following discontinuation of treatment. Encourage pregnant patients to participate in the Mycophenolate Pregnancy Registry
- Obtain a signed *Patient-Prescriber Acknowledgment Form* from females of reproductive potential
- Explain how your center will address the risks of mycophenolate-related first trimester pregnancy loss and congenital malformations

Please note that the program manufacturers may contact you in the future for assessment of Mycophenolate REMS.

This letter is not a comprehensive description of the risks associated with the use of mycophenolate. **For complete safety information, please see full *Prescribing Information*, including **Boxed WARNING** and *Medication Guide*, which can be found at [www.MycophenolateREMS.com](http://www.MycophenolateREMS.com).**

For more information about Mycophenolate REMS, including all program materials and instructions on how to enroll, please visit **[www.MycophenolateREMS.com](http://www.MycophenolateREMS.com)** or call **1-800-617-8191**.

The FDA requests healthcare providers to report any pregnancies of which they become aware. Pregnancies that occur during treatment with mycophenolate or within 6 weeks following discontinuation of treatment should be reported by contacting the Mycophenolate Pregnancy Registry.

- By phone: **1-800-617-8191**
- Online: **[www.MycophenolateREMS.com](http://www.MycophenolateREMS.com)**
- Or by mail: Mycophenolate Pregnancy Registry  
201 Broadway, Suite 5  
Cambridge, MA 02139

Thank you for your commitment to helping patients understand the risks and benefits associated with mycophenolate treatment.

Sincerely,

Mycophenolate REMS Team

**(Continued on next page)**



## IMPORTANT DRUG WARNING

Regarding Mycophenolate-Containing Products

### Indications and Important Selected Safety Information About Mycophenolate-Containing Products

#### INDICATIONS:

**CellCept® (mycophenolate mofetil)** is indicated for the prophylaxis of organ rejection in patients receiving allogeneic renal, cardiac or hepatic transplants. CellCept should be used concomitantly with cyclosporine and corticosteroids.

**Myfortic® (mycophenolic acid)** is indicated for the prophylaxis of organ rejection in patients receiving allogeneic renal transplants, administered in combination with cyclosporine and corticosteroids.

**Mycophenolate mofetil** is indicated for the prophylaxis of organ rejection in patients receiving allogeneic renal, cardiac or hepatic transplants. Mycophenolate mofetil should be used concomitantly with cyclosporine and corticosteroids.

**Mycophenolic acid** is indicated for the prophylaxis of organ rejection in patients receiving allogeneic renal transplants, administered in combination with cyclosporine and corticosteroids.

#### CONTRAINDICATIONS:

- Allergic reactions to mycophenolate-containing products have been observed; therefore, mycophenolate-containing products are contraindicated in patients with a hypersensitivity to mycophenolate mofetil, mycophenolic acid or any component of the drug product.
- CellCept Intravenous is contraindicated in patients who are allergic to Polysorbate 80 (TWEEN).

#### **WARNING: EMBRYOFETAL TOXICITY, MALIGNANCIES AND SERIOUS INFECTIONS**

**Use during pregnancy is associated with increased risks of first trimester pregnancy loss and congenital malformations. Females of reproductive potential (FRP) must be counseled regarding pregnancy prevention and planning.**

**Immunosuppression may lead to increased susceptibility to infection and possible development of lymphoma and other neoplasms. Only physicians experienced in immunosuppressive therapy and management of organ transplant recipients should prescribe mycophenolate-containing products. Patients receiving mycophenolate-containing products should be managed in facilities equipped and staffed with adequate laboratory and supportive medical resources. The physician responsible for maintenance therapy should have complete information requisite for the follow-up of the patient.**

(Continued on next page)

## IMPORTANT DRUG WARNING

Regarding Mycophenolate-Containing Products



### Important Selected Safety Information About Mycophenolate-Containing Products (cont'd)

#### WARNINGS:

##### Embryofetal Toxicity

- Mycophenolate-containing products can cause fetal harm when administered to a pregnant female. Use of mycophenolate-containing products during pregnancy is associated with an increased risk of first trimester pregnancy loss and an increased risk of congenital malformations, especially external ear and other facial abnormalities including cleft lip and palate, and anomalies of the distal limbs, heart, esophagus, and kidney.

##### Pregnancy Exposure Prevention and Planning

- Females of reproductive potential must be made aware of the increased risk of first trimester pregnancy loss and congenital malformations and must be counseled regarding pregnancy prevention and planning.

##### Lymphoma and Malignancy

- Patients receiving immunosuppressive regimens involving combinations of drugs, including mycophenolate-containing products, as part of an immunosuppressive regimen are at increased risk of developing lymphomas and other malignancies, particularly of the skin.

##### Combination with Other Immunosuppressive Agents

- Mycophenolate mofetil has been administered in combination with the following agents in clinical trials: antithymocyte globulin, OKT3, cyclosporine, and corticosteroids.
- Mycophenolic acid has been administered in combination with the following agents in clinical trials: antithymocyte/lymphocyte immunoglobulin, muromonab-CD3, basiliximab, daclizumab, cyclosporine, and corticosteroids.
- The efficacy and safety of the use of mycophenolate-containing products, in combination with other immunosuppressive agents have not been determined.

##### Serious Infections

- Patients receiving immunosuppressants, including mycophenolate, are at increased risk of developing bacterial, fungal, protozoal and new or reactivated viral infections, including opportunistic infections. These infections may lead to serious, including fatal outcomes.
- Polyomavirus associated nephropathy (PVAN), JC virus associated progressive multifocal leukoencephalopathy (PML), cytomegalovirus (CMV) infections, reactivation of hepatitis B (HBV) or hepatitis C (HCV) have been reported.

##### Neutropenia

- Severe neutropenia [absolute neutrophil count (ANC)  $<0.5 \times 10^3/\mu\text{L}$ ] developed in up to 2.0% of renal, up to 2.8% of cardiac, and up to 3.6% of hepatic transplant patients receiving mycophenolate mofetil 3g daily.
- Patients receiving mycophenolate-containing products should be monitored for neutropenia.
- If neutropenia develops [absolute neutrophil count (ANC)  $<1.3 \times 10^3/\mu\text{L}$ ] or anemia occurs, dosing with mycophenolate-containing products should be interrupted or the dose reduced, appropriate diagnostic tests performed, and the patient managed appropriately.

##### Pure Red Cell Aplasia

- Cases of pure red cell aplasia (PRCA) have been reported in patients treated with mycophenolate-containing products in combination with other immunosuppressive agents. Patients receiving mycophenolate-containing products should be monitored for blood dyscrasias.

**CAUTION: CELLCEPT INTRAVENOUS SOLUTION SHOULD NEVER BE ADMINISTERED BY RAPID OR BOLUS INTRAVENOUS INJECTION**

(Continued on next page)



## IMPORTANT DRUG WARNING

Regarding Mycophenolate-Containing Products

### Important Selected Safety Information About Mycophenolate-Containing Products (cont'd)

#### PRECAUTIONS:

##### Pregnancy Exposure Prevention and Planning

- Females of reproductive potential\* must be made aware of the increased risk of first trimester pregnancy loss and congenital malformations and must be counseled regarding pregnancy prevention and planning.
- Females of reproductive potential taking mycophenolate-containing products must receive contraceptive counseling and use acceptable contraception during entire therapy with mycophenolate-containing products and for 6 weeks after stopping therapy (see Full Prescribing Information for acceptable contraception methods).
- Patients should be aware that mycophenolate-containing products reduce blood levels of the hormones in the oral contraceptive pill and could theoretically reduce its effectiveness.
- To prevent unplanned exposure during pregnancy, females of reproductive potential should have a serum or urine pregnancy test with a sensitivity of at least 25 mIU/mL immediately before starting a mycophenolate-containing product.
- Another pregnancy test with the same sensitivity should be done 8 to 10 days later. Repeat pregnancy tests should be performed during routine follow-up visits.
- Results of all pregnancy tests should be discussed with the patient.
- In the event of a positive pregnancy test, females should be counseled with regard to whether the maternal benefits of mycophenolate treatment may outweigh the risks to the fetus in certain situations.
- For patients who are considering pregnancy, consider alternative immunosuppressants with less potential for embryofetal toxicity.

##### Pregnancy Category D

- Mycophenolate-containing products can cause fetal harm when administered to a pregnant female. If mycophenolate-containing products are used during pregnancy, or if the patient becomes pregnant while taking mycophenolate-containing products, the patient should be apprised of the potential hazard to the fetus. In certain situations, the patient and her healthcare practitioner may decide that the maternal benefits outweigh the risks to the fetus. Risks and benefits of mycophenolate-containing products should be discussed with the patient.
- For those females using mycophenolate-containing products at any time during pregnancy and those becoming pregnant within 6 weeks of discontinuing therapy, the healthcare practitioner should report the pregnancy to the **Mycophenolate Pregnancy Registry (1-800-617-8191)**. The healthcare practitioner should also strongly encourage the patient to enroll in the pregnancy registry.

##### Gastrointestinal Disorders

- Gastrointestinal bleeding (requiring hospitalization) has been reported in de novo renal transplant patients (1.0%) and maintenance patients (1.3%) treated with mycophenolic acid (up to 12 months); and in approximately 3% of renal, in 1.7% of cardiac and in 5.4% of hepatic transplant patients treated with mycophenolate mofetil 3g daily.
- Mycophenolate-containing products should be administered with caution in patients with active serious digestive system disease because mycophenolate-containing products have been associated with an increased incidence of digestive system adverse events.

##### Concomitant Medications

- It is recommended that mycophenolate-containing products not be administered concomitantly with azathioprine because of the potential to cause bone marrow suppression and inhibit purine metabolism.



**Important Selected Safety Information About Mycophenolate-Containing Products (cont'd)**

- Caution should be used in the concomitant administration of mycophenolate-containing products with drugs that interfere with enterohepatic recirculation such as cholestyramine because of the potential to reduce the efficacy of mycophenolate-containing products.

**Immunizations**

- During treatment with mycophenolate-containing products, avoid the use of live attenuated vaccines and advise patients that vaccinations may be less effective.

**Phenylketonurics**

- Care should be taken if mycophenolate mofetil oral suspension is administered to patients with phenylketonuria. Complete blood counts should be performed weekly during the first month, twice monthly for the second and third months of treatment, then monthly through the first year.

**Nursing Mothers**

- It is not known whether mycophenolate-containing products are excreted in human milk. Because many drugs are excreted in human milk, and because of the potential for serious adverse reactions in nursing infants from mycophenolate-containing products, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.
- Patients should not breastfeed during mycophenolate-containing products therapy.

\* A female of reproductive potential includes girls who have entered puberty and all women who have a uterus and have not yet passed through menopause.

**ADVERSE REACTIONS:**

- The principal adverse reactions associated with the administration of mycophenolate mofetil include diarrhea, leukopenia, sepsis, vomiting, and there is evidence of a higher frequency of certain types of infections, eg, opportunistic infections. Phlebitis and thrombosis have been reported with intravenous administration.
- The principal adverse reactions associated with the administration of mycophenolic acid include constipation, nausea, and urinary tract infection in de novo patients and nausea, diarrhea, and nasopharyngitis in maintenance patients.

**For additional safety information, please see full *Prescribing Information*, including **Boxed WARNING** and *Medication Guide*, which can be found at [www.MycophenolateREMS.com](http://www.MycophenolateREMS.com).**

# JOURNAL INFORMATION



IMPORTANT SAFETY INFORMATION FOR  
PRESCRIBERS OF MYCOPHENOLATE

# MYCOPHENOLATE REMS

## RISKS OF FIRST TRIMESTER PREGNANCY LOSS AND CONGENITAL MALFORMATIONS

Mycophenolate REMS (Risk Evaluation and Mitigation Strategy) has been mandated by the FDA (Food and Drug Administration) due to postmarketing reports showing that **exposure to mycophenolate during pregnancy is associated with increased risks of first trimester pregnancy loss and congenital malformations.**

### Mycophenolate is available by prescription as

- CellCept® (mycophenolate mofetil)
- Myfortic® (mycophenolic acid)
- Generic formulations of mycophenolate mofetil
- Generic formulations of mycophenolic acid

### The goals of Mycophenolate REMS are

1. To prevent unplanned pregnancy in patients using mycophenolate and to minimize fetal exposure to mycophenolate by informing prescribers and females of reproductive potential about
  - The increased risks of first trimester pregnancy loss and congenital malformations associated with exposure to mycophenolate during pregnancy; and
  - The importance of pregnancy prevention and planning
2. To minimize the risks associated with fetal exposure to mycophenolate by collecting information on pregnancy outcomes through the Mycophenolate Pregnancy Registry
3. To inform patients about the serious risks associated with mycophenolate

### What you need to know to prescribe mycophenolate

All prescribers of mycophenolate and females of reproductive potential, whether or not they plan to get pregnant, should participate in Mycophenolate REMS.

### Mycophenolate Pregnancy Registry

It is important for healthcare providers to report any pregnancies of which they become aware that occur during treatment with mycophenolate or within 6 weeks following discontinuation of treatment. The Mycophenolate Pregnancy Registry has been established to evaluate mycophenolate-exposed pregnancies and their outcomes. Pregnancies should be reported by contacting the Mycophenolate Pregnancy Registry at 1-800-617-8191.

Visit [www.MycophenolateREMS.com](http://www.MycophenolateREMS.com) or call 1-800-617-8191 to access all resource materials.

For complete safety information, please see full *Prescribing Information*, including Boxed WARNING and Medication Guide, which can be found at [www.MycophenolateREMS.com](http://www.MycophenolateREMS.com)

# OB/GYN CONTRACEPTION COUNSELING LETTER

((Date))

((Recipient's Name))

((Recipient's Address 1))

((Recipient's Address 2))

((City, State, ZIP))

In reference to: My patient ((Patient's Name))

Reason for the referral: Contraception counseling

Dear Dr ((Recipient's Last Name)):

I am writing to you in reference to the above-named patient who is under my care for ((diagnosis)) and ((insert drug information such as drug name, when patient will begin taking the drug, if treatment has already begun, etc)). This medication contains mycophenolate, which is associated with an increased risk of first trimester pregnancy loss and congenital malformations. It is important that this patient receive contraception counseling about methods that are acceptable for use while taking mycophenolate.

Prescribers of mycophenolate participate in the FDA-mandated Mycophenolate REMS (Risk Evaluation and Mitigation Strategy) to ensure that the benefits of mycophenolate outweigh the risks.

The following table lists the forms of contraception that are acceptable for use during treatment with mycophenolate.

### Acceptable Contraception Methods for Females of Reproductive Potential

Guide your patients to choose from the following birth control options:

<b>Option 1</b>  <b>Methods to Use Alone</b>	<ul style="list-style-type: none"><li>■ Intrauterine devices (IUDs)</li><li>■ Tubal sterilization</li><li>■ Patient’s partner had a vasectomy</li></ul>		
<b>OR</b>			
<b>Option 2</b>  <b>Choose One Hormone Method AND One Barrier Method</b>	<b>Hormone Methods choose 1</b>		<b>Barrier Methods choose 1</b>
	<b>Estrogen and Progesterone</b> <ul style="list-style-type: none"><li>■ Oral contraceptive pill</li><li>■ Transdermal patch</li><li>■ Vaginal ring</li></ul> <b>Progesterone-only</b> <ul style="list-style-type: none"><li>■ Injection</li><li>■ Implant</li></ul>	<b>AND</b>	<ul style="list-style-type: none"><li>■ Diaphragm with spermicide</li><li>■ Cervical cap with spermicide</li><li>■ Contraceptive sponge</li><li>■ Male condom</li><li>■ Female condom</li></ul>
<b>OR</b>			
<b>Option 3</b>  <b>Choose One Barrier Method From Each Column (must choose two methods)</b>	<b>Barrier Methods choose 1</b>		<b>Barrier Methods choose 1</b>
	<ul style="list-style-type: none"><li>■ Diaphragm with spermicide</li><li>■ Cervical cap with spermicide</li><li>■ Contraceptive sponge</li></ul>	<b>AND</b>	<ul style="list-style-type: none"><li>■ Male condom</li><li>■ Female condom</li></ul>

Patients should be aware that mycophenolate reduces blood levels of the hormones in the oral contraceptive pill and could reduce its effectiveness. An additional barrier method must be used with any hormonal contraceptives.

Patients should also be counseled on the availability of emergency contraception.

Unless patients choose not to have sexual intercourse with a man at any time (abstinence), they should be instructed to use acceptable birth control during the entire treatment with mycophenolate and for 6 weeks after they stop taking mycophenolate.

You can find more information about Mycophenolate REMS, including the roles and responsibilities of patients and prescribers of mycophenolate, at **[www.MycophenolateREMS.com](http://www.MycophenolateREMS.com)**. The site provides educational materials, as well as access to full *Prescribing Information*, *Important Safety Information* and *Medication Guides* for mycophenolate-containing products.

Please call me at ((Signatory's phone)) at your earliest convenience. Thank you for your cooperation.

Sincerely,

((Signatory's Name))

((Signatory's Practice))

# OB/GYN PRECONCEPTION COUNSELING LETTER

((Date))

((Recipient's Name))

((Recipient's Address 1))

((Recipient's Address 2))

((City, State, ZIP))

In reference to: My patient ((Patient's Name))

Reason for referral: Pre-conception counseling

Dear Dr ((Recipient's Last Name)):

I am writing to you in reference to the above-named patient who is under my care for ((diagnosis)) and ((insert drug information such as drug name, when patient will begin taking the drug, if treatment has already begun, etc)). This medication contains mycophenolate, and the patient is considering a pregnancy. Because exposure to mycophenolate during pregnancy is associated with increased risks of first trimester pregnancy loss and congenital malformations, it is important that this patient receive pregnancy planning education. There are three components to pregnancy planning which include the following:

1. Pre-conception counseling
2. Determining whether there are appropriate treatment options with less potential for embryofetal toxicity
3. Optimizing the patient's underlying medical conditions prior to conception

I would like you to provide pre-conception counseling in order to optimize the patient's future pregnancy outcome. Although a decision regarding treatment options with less potential for embryofetal toxicity may not have been made at the present time, these discussions will be done by my practice.

Prescribers of mycophenolate participate in the FDA-mandated Mycophenolate REMS (Risk Evaluation and Mitigation Strategy) to ensure that the benefits of mycophenolate outweigh the risks.

You can find more information about Mycophenolate REMS, including the roles and responsibilities of patients and prescribers of mycophenolate, at **www.MycophenolateREMS.com**. The site provides educational materials, as well as access to full *Prescribing Information*, *Important Safety Information*, and *Medication Guides* for mycophenolate-containing products.

I look forward to working with you to ensure that this patient receives appropriate pregnancy planning education. ((Insert any further details specific to this patient that the OB/GYN should know.))

Please call me at ((Signatory's phone)) at your earliest convenience. Thank you for your cooperation.

Sincerely,

((Signatory's Name))

((Signatory's Practice))

# MYCOPHENOLATE REMS HOMEPAGE

## WELCOME TO THE MYCOPHENOLATE REMS (Risk Evaluation and Mitigation Strategy)

### What is the Mycophenolate REMS?

The Mycophenolate REMS is a program to tell doctors, nurses, pharmacists and patients about the risks of taking mycophenolate during pregnancy. It was mandated by the Food and Drug Administration (FDA).

### What medications contain mycophenolate?

Mycophenolate Mofetil  
CellCept® by Genentech USA, Inc.

[Generic formulations by >>](#)

Mycophenolic Acid  
Myfortic® by Novartis Pharmaceuticals Corporation.

[Generic formulations by >>](#)

### Who should be informed about the Mycophenolate REMS?

- Doctors who prescribe mycophenolate.
- Females of reproductive potential\* who are taking mycophenolate.
- Pharmacists who dispense medicines with mycophenolate in them.



#### Prescribers

To enroll or order materials, [click here](#)



#### Pharmacists

For Pharmacists Overview [click here](#)



#### Patients

For Patient Overview, [click here](#)

### Why did the FDA mandate the Mycophenolate REMS?

The FDA determined that a REMS (Risk Evaluation and Mitigation Strategy) is necessary to ensure that the benefits of mycophenolate outweigh the risks of first trimester pregnancy loss and congenital malformations associated with mycophenolate use during pregnancy.

- Higher risk of miscarriage in the first 3 months.
- Higher risk that the baby will have birth defects.

### What are the goals of the Mycophenolate REMS?

The goals of the Mycophenolate REMS are:

- To prevent unplanned pregnancy in patients using mycophenolate and to minimize fetal exposure to mycophenolate by informing prescribers and females of reproductive potential about
  - the increased risks of first trimester pregnancy loss and congenital malformations associated with exposure to mycophenolate during pregnancy; and
  - the importance of pregnancy prevention and planning
- To minimize the risks associated with fetal exposure to mycophenolate by collecting information on pregnancy outcomes through the Mycophenolate Pregnancy Registry.
- To inform patients about the serious risks associated with mycophenolate.

\*Females of reproductive potential include girls who have entered puberty and all women who have a uterus and have not passed through menopause.

